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10/581,947

06/06/2006

Bertrand Leblond

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NIXON & VANDERHYE, PC  
901 NORTH GLEBE ROAD, 11TH FLOOR  
ARLINGTON, VA 22203

EXAMINER

BROOKS, CLINTON A

ART UNIT

PAPER NUMBER

1621

MAIL DATE

DELIVERY MODE

10/28/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/581,947	<b>Applicant(s)</b> LEBLOND ET AL.	
	<b>Examiner</b> CLINTON BROOKS	<b>Art Unit</b> 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22-41 is/are pending in the application.
- 4a) Of the above claim(s) 23, 26 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22, 24, 25, 27-30 and 32-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/6/2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/6/2006</u> .  | 6) <input type="checkbox"/> Other: _____                          |

***Priority***

Application no.10/581,947, filed June 6, 2006 is a national stage application of PCT/IB04/04334, filed December 10, 2004 which claims benefit of EPO03293143.8, filed December 12, 2003.

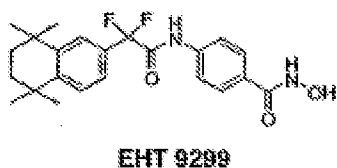
***Status of Claims***

Claims 22-41 are currently pending.

***Election Restriction***

1. Applicant's election with traverse of Group 13 and specie election of the compound below in the reply filed on September 25, 2009 is acknowledged. The traversal is on the ground(s) that unity of invention is present. This is not found persuasive because the special technical feature and or inventive concept linking the claims is not present. The rejection below illustrates that the special technical is present in the prior art. Therefore, unity of invention does not exist.

The requirement is deemed proper and is therefore made FINAL.



According to Applicant's claims 22, 24-25, 27-30, and 32-41 read on the elected specie. Claims 23, 26, and 31 are withdrawn from consideration pursuant to MPEP 803.02 as pertaining to a nonelected specie. After searching the elected specie was determined to be free of the art.

The search was expanded to a new specie (see rejection below).

***Information Disclosure Statement***

The Examiner has considered all references from the information disclosure statements (IDS) received June 6, 2006 that have not been marked with a strikethrough.

***Claim Objections***

**Claim 22** is objected to for the language “whenever possible”. The phrase is redundant. The objection can be removed by removing the phrase.

***Claim Rejections – 35 USC § 112/Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 22, 24-25, 24-25, 27-30, and 32-41** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 22, 24-25, 27-30, and 32-41 , the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The other claims depend either directly or indirectly from claim 22. This language is also found in at least claims 24, 27, and 33.

**Claims 22, 24-25, 27-30, and 32-41** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 recites the limitation "their salts" in the claim. There is insufficient antecedent basis for this limitation in the claim. To which potential salt is the claim referring? Is the salt for the specific group or the compound as a whole?

**Claims 22, 24-25, 27-30, and 32, 36-41** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 uses a proviso "or an ester derivative", amides are ester derivatives. As defined in claim 22, R is an amide, thus the claim includes and does not include amides.

**Claims 23** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "the groups identified in claim 1" is indefinite because it is unclear which groups have been identified. There are many "groups" within claim 22 such as "C1-6 alkyl group", "a fluoroalkyl group", "cyclic containing hydrocarbon group", "methyl or ethyl group", etc. Further, this claim is indefinite because there is no pending claim 1.

Art Unit: 1621

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

. **Claims 22, 24-25, 27-30, and 32-41**, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutically acceptable salts, does not reasonably provide enablement for hydrates or mixtures containing hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. The nature of the invention
2. The state of the prior art
3. The predictability or lack thereof in the art
4. The amount of direction or guidance present
5. The presence or absence of working examples
6. The breadth of the claims
7. The quantity of experimentation needed, and

Art Unit: 1621

8. The level of skill in the art

*The Nature of the Invention*

The invention relates to compounds that are HDAC inhibitors.

*The State of the Prior Art and the Predictability or lack thereof in the art*

Active pharmaceutical ingredients are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact, and generally stable format to store an active pharmaceutical ingredient or a drug product.

Understanding and controlling the solid-state chemistry of active pharmaceutical ingredients, both as pure drug substances and in formulated products, is therefore an important aspect of the drug development process. Active pharmaceutical ingredients can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals, and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability, and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms such as polymorphs and solvates are not so common to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them, and evaluate their properties as valuable new pharmaceutical materials. A large

Art Unit: 1621

number of factors can influence crystal nucleation and growth during this process, including the composition of the crystallization medium and the processes used to generate super-saturation and promote crystallization (Morissette et al. *Advanced Drug Delivery Reviews* 2004, 56, 275-300). Therefore, for these reasons, the state of the prior art is one of unpredictability.

As stated above, crystalline solids can exist in the form of polymorph, solvates or hydrates.

"Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate, and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug. Hence, it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development" (Vippagunta et al. *Advanced Drug Delivery Reviews* 2001, 48, 3-26, abstract). In further discussing the predictability of the formation of solvates, Vippagunta et al. discloses that "predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds" (page 18, section 3.4).

*The Amount of Direction or Guidance Present and Presence or Absence of Working Examples*

The only direction or guidance present in the instant specification is for compounds of claim 1, as well as pharmaceutically acceptable salts and pharmaceutical compositions. There is no data present in the specification for the preparation of hydrates of compounds of claim 1. The guidance in the specification is limited to the disclosure of generic definitions of compounds of



Art Unit: 1621

Formula (I) with the possible embodiments for each variable position on the compounds, with the mention of a "... salts, hydrates, and mixture thereof" however, it is not discussed which specific compounds can exist the hydrated or solvated form mentioned. Additionally, preferred embodiments and examples do not support enablement for hydrates of *specific* compounds. Finally, there are no working examples present in the disclosure for the preparation of solvates. In each of the working examples, the compound of Formula (I) is synthesized with no mention of particular solvates being produced for any example; in each example the solvent is removed for the purification of the desired compound.

*The Breadth of the Claims*

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any hydrates and solvates of the claimed compounds.

*The Quantity of Experimentation Needed and the Level of Skill in the Art*

While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to prepare *any* solvate of the compounds of claim 1. The science of crystallization has evolved such that, without guidance or working examples in the specification, the claims lack enablement. This rejection can be overcome by deletion of the words "hydrate or solvate" from claims 1 and 2.

. **Claims 37-41**, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds EHT9299, EHY7706, EHT7800, and EHT3741, does

Art Unit: 1621

not reasonably provide enablement for the use claims, which claim the use of the millions of compounds disclosed in the genus of formula I as HDAC inhibitors, treatment of central and peripheral nervous systems diseases or neurodegenerative diseases, treatment of fibrosis, cancer, or reducing cancer cell proliferation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

*The Nature of the Invention*

Claims 37-41 relate to a method for treatment of conditions mediated by HDAC such as cancer, psoriasis; treatment of central and peripheral nervous system diseases or neurodegenerative diseases; treatment of fibrosis; a variety of cancer types; and reducing cancer cell proliferation in all can cell lines.

*The State of the Prior Art and the Predictability or lack thereof in the art*

With respect to the state of the prior art the instant specification cites scientific articles and pending patent application that according to Applicants disclose:

1. That it is known that HDACS can catalyze the removing of the acetyl group from lysine residues in the N-terminus tails of nucleosomal core histones resulting in a more compact chromatin structure that is associated with repression of transcription.

Art Unit: 1621

2. That HDACs are involved in cell-cycle progression and differentiation; that the specific compounds--trichostatin A and SAHA are effective in a mice promyelocytic leukemia model.
3. Trichostatin A has been used in the treatment of fibrosis.
4. SAHA improves the motor impairment in R6/2 mice (a Huntington's disease model).
5. That HDAC inhibitors could be useful for treating diseases of the central nervous system in particular neurodegenerative diseases such as polyglutamine expansion diseases.

Further, the instant specification discloses that 9 human HDACs have been characterized and that two are inferred. Further, the instant specification discloses that two classes of HDACs are relevant because they are not NAD-dependent enzymes (Class I: HDAC 1,2,3,8; Class II, 4-6, and 7-10). Further, the instant disclosure states that SAHA inhibits both classes.

With respect to the lack of predictability in the art, the diseases recited in the instant claims represent a group with diverse etiologies. Further, there are many isoforms of the HDAC enzyme which are located in different locations within a cell--some in the nucleus and some in the nucleus and cytoplasm (instant specification page 2). As stated in the instant specification, different HDACs may be causative for different diseases.

Further, the instant specification discloses that active experimentation is ongoing stating that "[a] very few of small molecules are known that selectively target either of the two classes (class 1 or class 2) or individual members (HDAC 1-10) of the family) (page 2 of specification).

The combination of all these factors point to an early stage in the state of the art and a lack of predictability in the art.

Art Unit: 1621

*The amount of direction or guidance present and the presence or absence of working examples*

The specification discusses at page 64 that an HDAC activity assay was performed and that IC50 for 4 compounds were disclosed EHT9299, EHT7706, EHT7800, and EHT3741. Applicants' argue that these results illustrate the ability of the efficiency of the compounds of this invention to affect specifically HDAC enzymatic activity. No animal model for any disease model are presented. No data for an HDAC profile (all the HDAC enzymes or a cell line panel) against SAHA or trichostatin A that would suggest similar results based on similar HDAC inhibition is presented. Millions if not billions of compounds are presented.

*The breadth of the claims*

The claim is extremely broad in that it is drawn to the use of any compound of generic formula (I) for the treatment of any type of cancer, or other diseases as stated above.

*The level of the skill in the art*

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the inventions is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compound exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment of cancer and the other diseases recited, as a result necessitating one of skill to perform an exhaustive search for which compounds of the instant claims will be useful, if any, in order to practice the claimed invention.

*The quantity of experimentation needed*

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what compounds, if any, out of all compounds, would be effective in treating cancer and the other diseases

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compositions would treat cancer, psoriasis, central and peripheral nervous system diseases or neurodegenerative diseases, fibrosis, cancer cell proliferation in all cell lines with no assurance of success.

***Claim Rejections – 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

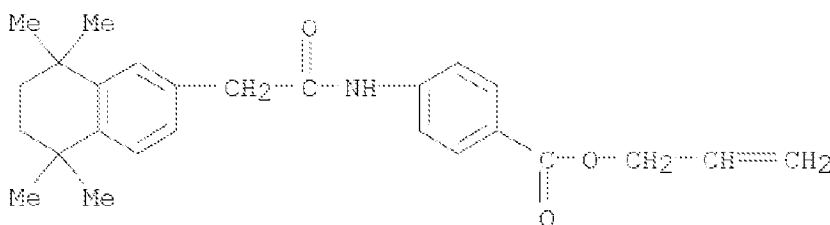
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. **Claims 22, 36** are rejected under 35 U.S.C. 102(b) as being anticipated by United States Patent No. 5567721 (“the ‘721 patent”).

4. The ‘721 patent teaches:

RN 142650-48-4 CAPLUS  
CN Benzoic acid, 4-[[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)acetyl]amino]-, 2-propen-1-yl ester (CA INDEX NAME)



5.

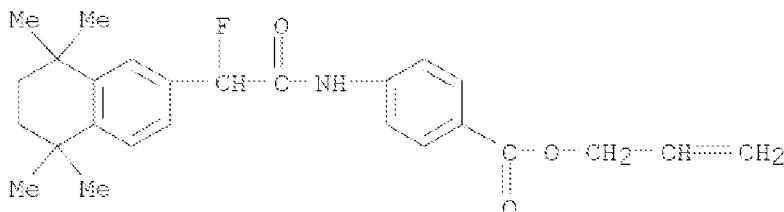
In this case R9 is an alkenyl group not an alkyl group (fully saturated) and therefore the proviso does not exclude this compound expanded specie).

Further, the ‘721 patent teaches at least the additional specie below:

Art Unit: 1621

RN 142651-02-3 CAPLUS

CN Benzoic acid, 4-[[2-fluoro-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)acetyl]amino]-, 2-propen-1-yl ester (CA INDEX NAME)



Further, the '721 teaches the following utilities (column 1, lines 9 to 20).

The present invention relates to new di(aromatic) compounds, to a process for preparing them and to their use in human and veterinary medicine and in cosmetics. 10

These new di(aromatic) compounds find application in the topical and systemic treatment of dermatological conditions linked to a disorder of keratinization (differentiation/proliferation) and dermatological or other conditions having inflammatory and/or immunoallergic components, and in degenerative diseases of connective tissue, and possess antitumour activity. In addition, these compounds may be used in the treatment of atopy, both cutaneous and respiratory, and of rheumatoid psoriasis. 15 20

They also find application in the ophthalmological field, in particular in the treatment of corneopathies.

### *Claim Rejections – 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness

rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1621

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

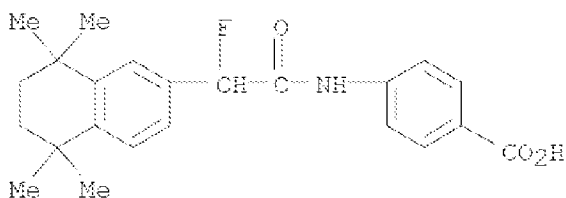
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. **Claims 22, 36-37, 40-41** are rejected under 35 U.S.C. 103(a) as being unpatentable over United States United States Patent No. 5567721 ("the '721 patent").

Further, the '721 patent teaches the following carboxylic acids:

RN 139611-91-7 CAPLUS  
 CN Benzoic acid, 4-[[2-fluoro-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)acetyl]amino]- (CA INDEX NAME)

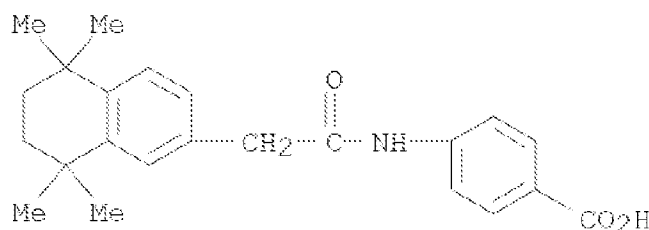




Art Unit: 1621

RN 142650-22-4 CAPLUS

CN Benzoic acid, 4-[[2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)acetyl]amino]- (CA INDEX NAME)



The proviso language excludes carboxylic acids, however, the '721 patent teaches:

(86) In the case where R.sub.1 represents a --COOH radical, the compounds are preferably prepared by protecting R.sub.1 with an allyl protective group. Conversion to the free form is performed by means of a catalyst such as tetrakis (triphenylphosphine) palladium(0) in the presence of a secondary amine (morpholine).

(87) The acids thereby obtained may be converted in a known manner to the corresponding acid chloride which, when treated with an alcohol (R.sub.6 OH) or an amine HN(r')(r''), gives the corresponding ester or amide (column 6, lines 35 to 44).

The '925 patent teaches that r' and r'' of the amide can be (column 2, lines 16 to 22):

r' and r'', which may be identical or different, representing a hydrogen atom, a lower alkyl radical, an aryl radical, an aralkyl radical, an amino acid residue, a sugar residue, an amino sugar residue or a heterocycle, or r' and r'' taken together form a heterocycle.

Thus, the '925 patent teaches at least that R is another Zn chelating group.

Further, the '925 patent teaches that these compounds have utility against cancer cells.

These compounds exhibit good activity in the test of differentiation of mouse embryonic teratocarcinoma cells (F9) (Cancer Research 43, p. 5268, 1983) and/or in the test of

Art Unit: 1621

ornithine decarboxylase inhibition after induction by "tape stripping" in nude rats (Lab. Animals 1, p. 233-240, 1987) or by TPA in mice (Cancer Research 8, p. 793-801, 1978). These tests show the activities of the compounds in the fields of differentiation and of proliferation, respectively.

The '925 patent fails to teach a specific example of the carboxylic acid above as an amide.

However, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to synthesize amides as disclosed in '925 patent with an expectation of success because the '925 patent suggests their synthesis and structurally similar compounds are expected to have similar properties. MPEP 2144.09 states: A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979).

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CLINTON BROOKS whose telephone number is (571)270-7682. The examiner can normally be reached on Monday-Friday 8:00 AM to 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, DANIEL SULLIVAN can be reached on (571)272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1621

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cab

/Daniel M Sullivan/

Supervisory Patent Examiner, Art Unit 1621